

AMENDMENTS TO THE SPECIFICATION

Please replace the paragraph starting with “FIGURE 2 – ” on lines 12-13 of page 3, with the following paragraph:

FIGURE 2 - Amino acid sequence composition correspondent to the S-1 region of the α -MHC in rat (SEQ ID NO:32) and mouse (SEQ ID NO:33).

Please replace the paragraph starting with “*Recombinant wild type and mutant smooth muscle HMMs.*” on lines 13-18 of page 26, with the following paragraph:

Recombinant wild type and mutant smooth muscle HMMs. Amino acid composition of the recombinant wild type (SEQ ID NO:1) and mutant (SEQ ID NO:2) smooth muscle generated in this study were confirmed by DNA sequencing. The expressed mutation of G343S occurs in an otherwise conserved residue.

WT	Ch Sm	341	I M G F T E E E Q T (<u>SEQ ID NO:1</u>)
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Mutant	Ch Sm	341	I M S F T E E E Q T (<u>SEQ ID NO:2</u>)
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Please replace the paragraph at lines 16-23 of page 51 with the following:

Following is a comparison of the loop 1 regions of the mouse cardiac α MHC cDNA (SEQ ID NO:3) and the corresponding amino acid sequence (SEQ ID NO:4) and the rat/pig β MHC cDNA (SEQ ID NO:5) and the corresponding amino acid sequence (SEQ ID NO:6):

mouse α MHC

(SEQ ID NO:3) 694 att gca gcc ata ggg gac cgt agc aag aag gaa aat cct aat gca aac aag ggc acc ctg gag g 757
(SEQ ID NO:4) 198 I A A I G D R S K K E N P N A N K G T L E -

pig β MHC

(SEQ ID NO:5) 602 att gct gcc att ggg gac cgc agc aag aag gac cag acc c-- -ca ggc aag ggc acc ttg gaa g 662
(SEQ ID NO:6) 198 I A A I G D R S K K D Q T P G K G T L E -

Please replace the paragraph at lines 1-6 of page 52 with the following:

Oligonucleotide primers that allow substitution of the rat/pig β MHC loop 1 for the mouse cardiac α MHC loop 1 in the α MHC gene were synthesized (SEQ ID NO:7). Capitalized nucleotides represent the exon 7 sequence; lower case letters represent intronic sequence. Translationally silent nucleotide substitutions (bolded in the DNA sequence shown below) allowed the introduction of a novel Pvu I restriction site.

Please delete the paragraph at lines 14-18 of page 53, consisting of the image and the caption.

Please replace the paragraph bridging line 15 of page 54 to line 25 of page 55 with the following:

The inventors have also performed a comparison of loop 1 sequences in myosin heavy chain isoforms. Given the putative role of loop 1 in determining kinetic properties of myosin, the inventors studied the loop in various myosins as an important step in investigating whether sequence variations might account for the differing characteristics of

SKELETAL MHC ISOFORMS

		204																	216
(SEQ ID NO:8)	chick pect	E K	K K E E	Q	-	S	G	K	M	Q	G	T	L	E	D				
(SEQ ID NO:9)	human/pig 2a	E K	K K E E	P	T	S	G	K	M	Q	G	T	L	E	D				
(SEQ ID NO:10)	human 2x	E K	K K E E	V	T	S	G	K	M	Q	G	T	L	E	D				
(SEQ ID NO:11)	rabbit 2x	D K	K K E E	A	T	S	G	K	M	Q	G	T	L	E	D				
(SEQ ID NO:12)	rabbit 2b	D K	K K E E	P	T	P	G	K	M	Q	G	T	L	E	D				

CARDIAC MHC ISOFORMS

(SEQ ID NO:13)	human α	D R	S K K D N	A	N	A	-	N	K	G	T	L	E	D
(SEQ ID NO:14)	rat α	D R	S K K D N	P	N	A	-	N	K	G	T	L	E	D
(SEQ ID NO:15)	mouse α	D R	S K K E N	P	N	A	-	N	K	G	T	L	E	D
(SEQ ID NO:16)	human β	D R	S K K D Q	S	P	G	-	-	K	G	T	L	E	D
(SEQ ID NO:17)	pig β	D R	S K K D Q	T	P	G	-	-	K	G	T	L	E	D
(SEQ ID NO:18)	rat β	D R	S K K D Q	T	P	G	-	-	K	G	T	L	E	D

~~Sequences corresponding to loop 1 in various MHC isoforms, aligned according to the chicken pectoralis numbering of Rayment, *et al.* (51). The sequences of human 2a, pig 2a, human 2x, rabbit 2x, rabbit 2b, pig β cardiac and rabbit β cardiac and were obtained in our laboratory as predictions from cDNA's generated by RT-PCR/cloning of electrophoretically characterized myocytes (53) and subsequent sequencing. The rest are gene bank sequences.~~

these isoforms. The inventors have cloned and sequenced the part of the MHC gene that encodes this domain in isoforms from various species. Sequences corresponding to loop 1 in various

MHC isoforms, aligned according to the chicken pectoralis numbering of Rayment, *et al.* (51).

The sequences of human 2a, pig 2a, human 2x, rabbit 2x, rabbit 2b, pig β cardiac and rabbit β cardiac and were obtained in our laboratory as predictions from cDNA's generated by RT-PCR/cloning of electrophoretically characterized myocytes (53) and subsequent sequencing.

The rest are gene bank sequences. The following conclusions may reasonably be drawn from these comparisons:

Please replace the paragraph bridging from line 15 of page 59 to line 19 of page 60 with the following:

	316	317	318	319	320	321	322	323	324	325	326	327	328	329
(SEQ ID NO:19) Chicken Pect	S	<u>E</u>	G	E	I	T	V	<u>P</u>	S	I	D	D	Q	E
(SEQ ID NO:20) Rat β Card	-	Q	-	-	T	-	-	A	-	-	-	-	S	-
(SEQ ID NO:21) Hum β Card	-	Q	-	-	T	-	-	A	-	-	-	-	A	-
(SEQ ID NO:22) Pig β Card	-	Q	-	-	T	-	-	A	-	-	-	-	A	-
(SEQ ID NO:23) Rat α Card	-	Q	-	-	V	S	-	A	-	-	-	-	S	-
(SEQ ID NO:24) Mouse α Card	-	Q	-	-	V	S	-	A	-	-	-	-	S	-
(SEQ ID NO:25) Rabbit 2x	-	-	-	-	-	-	-	-	-	-	-	-	S	-

	330	331	332	333	334	335	336	337	338	339	340	341	342	343
(SEQ ID NO:19) Chicken Pect	E	L	M	A	T	D	S	A	I	D	I	L	G	F
(SEQ ID NO:20) Rat β Card	-	H	-	-	-	-	-	-	F	-	V	-	-	-
(SEQ ID NO:21) Hum β Card	-	-	-	-	-	-	N	-	F	-	V	-	-	-
(SEQ ID NO:22) Pig β Card	-	-	-	-	-	-	N	-	F	-	V	-	-	-
(SEQ ID NO:23) Rat α Card	-	-	L	-	-	-	-	-	F	-	V	-	-	-
(SEQ ID NO:24) Mouse α Card	-	-	L	-	-	-	-	-	F	-	V	-	S	-
(SEQ ID NO:25) Rabbit 2x	-	-	-	-	-	-	-	-	-	-	-	-	-	-

	344	345	346	347	348	349	350	351	352	353	354	355	356	357
(SEQ ID NO:19) Chicken Pect	S	A	D	E	GAP	T	A	I	Y	GAP	L	T	G	A
(SEQ ID NO:20) Rat β Card	T	<u>P</u>	E	-	K	N	S	I	-	K	-	-	-	-
(SEQ ID NO:21) Hum β Card	T	S	E	-	-	N	S	M	-	-	-	-	-	-
(SEQ ID NO:22) Pig β Card	T	S	E	-	-	N	S	M	-	-	-	-	-	-
(SEQ ID NO:23) Rat α Card	T	-	E	-	-	A	G	V	-	-	-	-	-	-
(SEQ ID NO:24) Mouse α Card	T	-	E	-	-	A	G	V	-	-	-	-	-	-
(SEQ ID NO:25) Rabbit 2x	T	S	-	-	R	V	S	-	-	-	-	-	-	-

Please replace the paragraph at lines 4-8 on page 64 with the following:

EXON 11

(SEQ ID NO:26) Mouse α A S I D D S E E L L A T D

(SEQ ID NO:27) Pig β A S I D D S E E L M A T D

(SEQ ID NO:28) Rat β A S I D D S E E H M A T D

EXON 12

(SEQ ID NO:29) Mouse α S A F D V L S F T A E E K A G V

(SEQ ID NO:30) Pig β N A F D V L G F T A E E K N G V

(SEQ ID NO:31) Rat β S A F D V L G F T P E E K A S I